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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/593,993

10/27/2006

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442P106

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06/18/2008

EXAMINER

DICKINSON, PAUL W

ART UNIT

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1618

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/593,993	<b>Applicant(s)</b> TABATA ET AL.	
	<b>Examiner</b> PAUL DICKINSON	<b>Art Unit</b> 1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 17 March 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-3 and 5-23 is/are pending in the application.
- 4a) Of the above claim(s) 16-23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3 and 5-15 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 22 September 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>1/12/2007</u> .   | 6) <input type="checkbox"/> Other: _____                          |

**prDETAILED ACTION**

***Election/Restrictions***

Applicant's election of Group I in the reply filed on 3/17/2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "modified substances thereof" renders the claim indefinite. It is unclear how far removed the molecular structure of the "modified substance" can be from the parent compound without being considered an entirely different compound altogether.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5, 7, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by US 6355225 (hereafter '225). '225 discloses a water-soluble C<sub>60</sub> fullerene wherein the fullerene has a functional group in the molecule and a water-soluble polymer is linked through the functional group; wherein said functional group is a carboxyl group (see abstract; col 3, line 53 to col 4, line 3; col 8, lines 23-67). The water-soluble polymers include polypeptides and polyethylene glycol (see *ibid*). The water-soluble fullerenes are dissolved in an aqueous solution (see col 4, line 23 to col 7, line 33).

Claims 1-3, 5-8, 13 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Sun et al (Sun et al, Preparation and Characterization of Highly Water-soluble Pendant Fullerene Polymers, 1999, 32, 8747-8752). Sun et al discloses a water-soluble C<sub>60</sub> fullerene wherein the fullerene has a functional group in the molecule and poly(propionyl-ethylenimine-co-ethylenimine (a water-soluble polymer) is linked through the functional group; wherein said functional group is a carboxyl group (see abstract; Experimental Section). The polymer has a molecular weight of ~50,000 daltons (see Materials). The water-soluble fullerene is evaporated from solution as a solid, which the Examiner is interpreting as a form of an aggregate (see Pendant MFCA-PPEI and Pendant MFPCA-PPEI). The aggregate was broken apart via sonication to dissolve the sample in water (see aqueous solubility).

Claims 1-3, 5-8, and 13-15 are rejected under 35 U.S.C. 102(e) as being anticipated by US 20050143327 (hereafter '327). '327 discloses a water-soluble C<sub>60</sub>

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fullerene wherein the fullerene has a functional group in the molecule and a water-soluble polymer is linked through the functional group; wherein said functional group is a carboxyl group (see abstract; ¶ 13-18; Figures 1-5 and 11-19). The polymers disclosed have an inactive group at one end and a reactive group at the other (for Example, see Figure 3). The water-soluble fullerene can be in aggregate form or dissolved in water (see Example 1). The aggregate particles have a size of 100 to 400 nm (see ¶ 138).

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

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were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 5-11, 13, and 15 are rejected under 35 U.S.C. 103(a) as being anticipated by Tabata et al (Tabata et al, Antitumor effect of poly(ethylene glycol) modified fullerene, Fullerene Science and Technology, 1997, 5(5), 989-1007) in view of 6355225 (hereafter '225). Tabata et al discloses a water-soluble C<sub>60</sub> fullerene wherein the fullerene has a functional group in the molecule and polyethylene glycol (a water-soluble polymer) is linked through the functional group (see Introduction; Materials and Methods). The polyethylene glycol has a molecular weight of 5,460 daltons and is terminated by a methoxy group on one end and an amine group on the other (see Materials and Methods, Materials). Instant Claim 10 requires a C1-6 alkyl group at one end. Polyethylene glycol has the formula  $-(CH_2CH_2O)_n-$  and when it is terminated by a methoxy group, this is the equivalent of being terminated by a methyl group, i.e.  $-(CH_2CH_2O)_nMe$ . The fullerene compounds are potential drugs for use in anti-tumor therapy (see abstract). Tabata et al fails to disclose using a carboxyl functional group to link the polyethylene glycol to the fullerene.

'225 discloses that it is known that water-soluble polymers with terminal amines can be readily linked to fullerenes using carboxyl functional groups (see abstract; col 3,

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line 53 to col 4, line 3; col 8, lines 23-67). Specifically, malonic acid groups can be readily added to the fullerene using the Bingle-Hirsch reaction. The fullerene is subsequently reacted with the amine terminated polymer thereby attaching fullerene to the polymer (see *ibid*). This method is convenient, and produces soluble, non-toxic fullerene compounds useful for administration to patients.

It would be obvious to one of ordinary skill in the art at the time the invention was made to link the amine terminated polyethylene glycol to C<sub>60</sub> disclosed by Tabata et al, using carboxyl functional groups, with a reasonable expectation of success. Specifically, it would be reasonable to link the amine terminated polyethylene glycol to C<sub>60</sub> disclosed by Tabata et al using the method disclosed by '225, to afford a soluble, non-toxic fullerene compound. In this way, the amine terminated polyethylene glycol can be conveniently attached to the fullerene producing a compound with an improved anti-tumor efficacy.

Claims 1-3, 5-12, and 15 are rejected under 35 U.S.C. 103(a) as being anticipated by Tabata et al (see above) in view of 6355225 (hereafter '225) in further view of Conover et al (Conover et al, Camptothecin delivery systems: the utility of amino acid spacers for the conjugation of camptothecin with polyethylene glycol to create prodrugs, *Anti-Cancer Drug Design*, 1999, 14, 499-506). The relevant portions of Tabata et al and '225 are described above in the rejection of Claims 1-3, 5-11, 13, and 15 under 35 U.S.C. 103(a). Tabata et al fails to disclose a polyethylene glycol-amino acid conjugate as disclosed in Instant Claim 12.

Conover et al discloses camptothecin prodrugs wherein the drug is linked to a polyethylene glycol-amino acid conjugate and the use of the compound in anti-tumor therapy (see abstract; Materials and Methods). The polyethylene glycol-amino acid conjugate provide the otherwise hydrophobic compound with enhanced water solubility, non-toxicity, and thereby increases the anti-tumor efficacy of the compound (see Results and Discussion).

Tabata et al and Conover et al directed to the same field of endeavor, namely, anti-tumor drugs. It would be obvious to one of ordinary skill in the art to substitute the polyethylene glycol disclosed by Tabata et al with a polyethylene glycol-amino acid conjugate as disclosed by Conover et al, with a reasonable expectation of success, to afford a water-soluble fullerene with enhanced water solubility, non-toxicity, and thereby increasing the anti-tumor efficacy of the fullerene.

### ***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL DICKINSON whose telephone number is (571)270-3499. The examiner can normally be reached on Mon-Thurs 9:00am-6:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/  
Supervisory Patent Examiner, Art Unit 1618

Paul Dickinson  
Examiner  
AU 1618

June 5, 2008